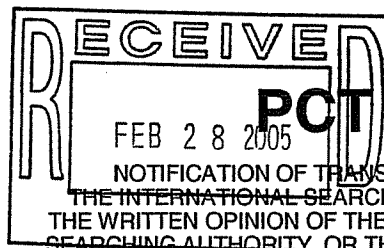


PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:

JENKINS, WILSON & TAYLOR, P.A.
University Tower
Attn. Taylor Jr., Arles A.
3100 Tower Boulevard Suite 1400
Durham NC 27707
UNITED STATES OF AMERICA



(PCT Rule 44.1)

Date of mailing
(day/month/year)

21/02/2005

Applicant's or agent's file reference

297/176 PCT

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US2004/036178

International filing date
(day/month/year)

01/11/2004

Applicant

NORTH CAROLINA STATE UNIVERSITY

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

DOCKET DATES: 3/21, 4/16, 4/21/05

ASSIGNED ATT: AATJWC

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

FILE NO. 297/176 PCT

Gwenaelle Elorica

DOCKETED BY: HMD

DATE: 3.1.05

* 5.21.05 = Dd1 to file

IDS in

US.

(see notes on accompanying sheet)

✓ SHS
21-05

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| | | |
|--|---|---|
| Applicant's or agent's file reference 297/176 PCT | FOR FURTHER ACTION <div style="float: right; font-size: small;">see Form PCT/ISA/220 as well as, where applicable, Item 5 below.</div> | |
| International application No. PCT/US2004/036178 | International filing date (day/month/year) 01/11/2004 | (Earliest) Priority Date (day/month/year) 30/10/2003 |
| Applicant NORTH CAROLINA STATE UNIVERSITY | | |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

a. the figure of the **drawings** to be published with the abstract is Figure No. 2

☐ as suggested by the applicant.

☒ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/036178

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| A | PARK S-J ET AL: "ARRAY-BASED ELECTRICAL DETECTION OF DNA WITH NANOPARTICLE PROBES" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 295, 22 February 2002 (2002-02-22), pages 1503-1506, XP001160895 ISSN: 0036-8075 abstract; figure 1 | |
| A | US 2003/044805 A1 (MIRKIN CHAD A ET AL) 6 March 2003 (2003-03-06) A method to detect target nucleic acids using oligonucleotides labelled with nanoparticles, which oligonucleotides are complementary to the nucleic acids paragraph '0024! | |
| | ----- -/-- ----- | |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Z document member of the same patent family

Date of the actual completion of the international search

3 February 2005

Date of mailing of the international search report

21/02/2005

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Bort, S

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2004/036178

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|---|-----------------------|
| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| A | KAI ERIKO ET AL: "Detection of PCR products of Escherichia coli 0157:H7 in human stool samples using surface plasmon resonance (SPR)" FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, vol. 29, no. 4, December 2000 (2000-12), pages 283-288, XP002316134 ISSN: 0928-824, figure 1 | |
| P,X | LOWE LISA B ET AL: "Laser-induced temperature jump electrochemistry on gold nanoparticle-coated electrodes" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 125, no. 47, 26 November 2003 (2003-11-26), pages 14258-14259, XP002316112 ISSN: 0002-7863 the whole document | 1-50 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/036178

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---------------------|----------------------------|---------------------|
| US 2003044805 | A1 | 06-03-2003 | |
| | | US 6506564 B1 | 14-01-2003 |
| | | US 6361944 B1 | 26-03-2002 |
| | | AU 774593 B2 | 01-07-2004 |
| | | AU 3279501 A | 24-07-2001 |
| | | AU 5520301 A | 08-10-2001 |
| | | CA 2396113 A1 | 19-07-2001 |
| | | CA 2402955 A1 | 04-10-2001 |
| | | EP 1294930 A2 | 26-03-2003 |
| | | EP 1301625 A2 | 16-04-2003 |
| | | JP 2004501340 T | 15-01-2004 |
| | | JP 2004515208 T | 27-05-2004 |
| | | US 2003087242 A1 | 08-05-2003 |
| | | WO 0151665 A2 | 19-07-2001 |
| | | WO 0173123 A2 | 04-10-2001 |
| | | US 2003207296 A1 | 06-11-2003 |
| | | US 2003180783 A1 | 25-09-2003 |
| | | US 2004072231 A1 | 15-04-2004 |
| | | US 2004110220 A1 | 10-06-2004 |
| | | US 2002155442 A1 | 24-10-2002 |
| | | US 2002172953 A1 | 21-11-2002 |
| | | US 2003059777 A1 | 27-03-2003 |
| | | US 2003049630 A1 | 13-03-2003 |
| | | US 2002146720 A1 | 10-10-2002 |
| | | US 2002164605 A1 | 07-11-2002 |
| | | US 2002182611 A1 | 05-12-2002 |
| | | US 2002155458 A1 | 24-10-2002 |
| | | US 2002137070 A1 | 26-09-2002 |
| | | US 2002127574 A1 | 12-09-2002 |
| | | US 2002137071 A1 | 26-09-2002 |
| | | US 2003049631 A1 | 13-03-2003 |
| | | US 2003143538 A1 | 31-07-2003 |
| | | US 2002155459 A1 | 24-10-2002 |
| | | US 2003054358 A1 | 20-03-2003 |
| | | US 2002160381 A1 | 31-10-2002 |
| | | US 2002155461 A1 | 24-10-2002 |
| | | US 2002155462 A1 | 24-10-2002 |
| | | US 2003124528 A1 | 03-07-2003 |
| | | US 2002137072 A1 | 26-09-2002 |
| | | US 6812334 B1 | 02-11-2004 |
| | | US 2003068622 A1 | 10-04-2003 |
| | | US 2004219520 A1 | 04-11-2004 |
| | | US 2003148282 A1 | 07-08-2003 |
| | | US 2002182613 A1 | 05-12-2002 |
| | | AU 5637800 A | 31-01-2001 |
| | | CA 2376623 A1 | 04-01-2001 |
| | | EP 1198591 A1 | 24-04-2002 |
| | | JP 2003503699 T | 28-01-2003 |
| | | WO 0100876 A1 | 04-01-2001 |
| | | US 6495324 B1 | 17-12-2002 |
| | | US 6417340 B1 | 09-07-2002 |

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

To:

see form PCT/ISA/220

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2004/036178

International filing date (day/month/year)
01.11.2004

Priority date (day/month/year)
30.10.2003

International Patent Classification (IPC) or both national classification and IPC
C12Q1/68

Applicant
NORTH CAROLINA STATE UNIVERSITY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

DOCKET DATES: 3/21, 4/16, 4/21/05
 ✓ ASSIGNED ATTY: AAT/JWC
 FILE NO. 297/176 PCT
 DOCKETED BY: HMD
 DATE: 3.1.05
 * 5.21.05 = Dd1 to file IDS
 in us. ✓ sub 3-1-05

Name and mailing address of the ISA:



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Bort, S

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/036178

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/036178

Box No. II Priority

1. ☐ The following document has not been furnished:

☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☒ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-50 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-50 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-50 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

Reference is made to the following documents:

- D1: Lowe et al. 'Laser-induced temperature jump electrochemistry on gold nanoparticle-coated electrodes' (26.11.2003) JOURNAL OF THE AMERICAN CHEMICAL SOCIETY (125):14258-14259
- D2: Park et al. 'ARRAY-BASED ELECTRICAL DETECTION OF DNA WITH NANOPARTICLE PROBES' (22-02-2002) SCIENCE, 295 (22):1503-1505:
- D3: US2003/0044805 (06.03.2003) NANOSPHERE, INC.
- D4: KAI E. ET AL 'Detection of PCR products of Escherichia coli O157:H7 in human stool samples using surface plasmon resonance (SPR)' (2000) FEMS IMMUNOLOGY AND MEDICAL MICROBIOLOGY, 29:283-288

RE Item II

D1 is published on 23.11.2004. Although D1 does not constitute prior art within the meaning of Rule 64.1(b) PCT, it appears to disclose all the features of independent claim 1. The priority document pertaining to the present application was not available at the time of establishing the present communication. Hence, it is based on the assumption that all the claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, D1 could become relevant to assess whether the claimed subject matter satisfy the criteria set forth in Art. 33(1) PCT.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Clarity

According to the present wording of the claims, the method of claim 1
Dependent claim 15 refers to the method of claim 1, wherein the detection . However,

in the method of claim 1 no detection probe is used.

Dependent claim 28 relates to a method wherein a plurality of different capture probes are used. Dependent claim 29 relates to the method of claim 28 wherein each attachment point of the array is separately exposed to light. However, since it appears that a separate exposition to light is the only feasible way to perform the method of dependent claim 25, said feature should be included in claim 29 and not formulated in a different dependent claim.

The terms *rastering* and *sacrificial electron donor* used in dependent claims 31 and 32, respectively, are unclear, rendering the scope of protection of said claims unclear.

The feature of dependent claim 45, namely that 'the nanoparticle is attached to the target sequence', is already present in the independent claim to which claim 45 refers back. This redundancy of features renders unclarity to the scope of protection of the claims.

According to page 11, lines 3-5 in the description, in the method of claim 1, the electric changes are the result of the laser-induced temperature jumps involving nanoparticles plasmon excitations. However, according to other parts of the description, i.e. page 15, first full paragraph, "some embodiments (...) are free of the use of a target analyte attached to a conductive support and/or a nanoparticle comprising a photoelectrochemically active moiety...". The above contradiction renders unclear the scope of protection of the claims.

It is clear from the description on page 10, lines 20-24, that the nanoparticles used in the method of claim 1 must have plasmon resonances in the region of the light used. Since independent claim 1 does not contain this feature it does not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

Should the above-mentioned lack of clarity objections be overcome, the following opinion on novelty and inventive step for the subject-matter of claims 1-50 would apply:

Novelty

D2 and D3 disclose an array-based electrical detection of DNA with nanoparticle probes. In said method DNA target molecules are detected using an array of capture probes located between two minielectrodes. Gold nanoparticle-labelled detection probes are hybridised to the immobilised target DNA, resulting in change in the conductivity between the electrodes (cf. page 1197, Box 1; paragraph [0024], respectively).

D4 discloses a method for detecting PCR products using a surface plasmon resonance (SPR) BIACON device and peptide nucleic acid as sensor probes (cf. abstract and fig. 1).

Claims 1-50 are, hence, novel over cited prior art.

Inventive step

Document D2 is considered to represent the most relevant state of the art for the method of independent claim 1. D2 discloses a method to identify DNA target molecules. In said method the target nucleic acids are hybridised to an array of capture probes located between two minielectrodes. Gold nanoparticle-labelled detection probes are hybridised to the immobilised target DNA, resulting in change in the conductivity between the electrodes (cf. abstract).

The subject-matter of independent claim 1 differs in that the nanoparticle is exposed to light having a wavelength absorbed by the nanoparticle.

The technical effect of the method of claim 1 would be the identification of very low concentrations, in the order of 100fM, of DNA molecules in a sample.

The problem to be solved by the subject matter of claim 1 may therefore be regarded as the provision of a more sensitive detection method.

The solution would be to irradiate the hybridisation complex with light and detect the electrical signal.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/036178

This solution can be considered as involving an inventive step for the following reasons: cited prior art documents D2 and D3 disclose the use of nanoparticles to detect DNA molecules, based on a change in conductivity due to the nanoparticles localise in the electrode gap and the silver deposition. Cited prior art document D4 discloses a method to detect DNA molecules based on surface plasmon resonance (SPR). In said method, the target nucleic acid is detected due a change in the refractive index at the surface, resulting from the SPR (cf. fig. 1). However, none of the cited prior art documents discloses the possibility of using light-induced temperature electrochemistry, associated with SPR, and nanoparticles to detect the presence of a target nucleic acid. Consequently, the Examining Division is of the opinion that application of light-induced temperature electrochemistry and nanoparticles in DNA detection methods involves the use of inventive skills.

The present application does meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1-50 does involve an inventive step in the sense of Article 33(3) PCT.